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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,116	07/07/2003	Daniel A. Coleman	CYT0P111	9130

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EXAMINER

NEGIN, RUSSELL SCOTT

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/615,116	Applicant(s) COLEMAN ET AL.	
	Examiner Russell S. Negin	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/13/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 102

The rejections of claims 1-13, 17-20, 22-23, 28-33, 37-38, 43-47 under 35 U.S.C. 102(b) as being anticipated by Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] are withdrawn due to amendments made by the applicants to the set of claims filed on 13 July 2006.

Claim Rejections - 35 USC § 103

The rejections of claims 15, 16, 35, 36, 48-50, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al [Cytometry, volume 13, pages 404-415, 1992] in view of Koss et al. [American Journal of Clinical Pathology, 1998, volume 109, pages 549-557] are withdrawn due to amendments made by the applicants to the set of claims filed on 13 July 2006.

The rejections of claims 23-25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al [Cytometry, volume 13, 1992, pages 404-415] in view of Rumbaugh [USPAT 4,821,210] are withdrawn due to amendments made by the applicants to the set of claims filed on 13 July 2006.

The rejections of claims 23 and 24 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al [Cytometry, volume 13, 1992, pages 404-415] in view of Miyano et al [USPGPUB 2003/0108230] are withdrawn due to amendments made by the applicants to the set of claims filed on 13 July 2006.

Art Unit: 1631

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus [US Patent 4,741,043].

Claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 claim an automated method, computer device, or media for "automatically" identifying binuclear cells with each dependent claim claiming a different feature or parameter to restrict the independent claim.

In Gerlyng et al. Figure 1A and Table 1, the authors describe a method for identifying bi-nuclear cells by capturing an image of a plurality of marked cells. As stated on page 406, column 1, lines 22-30 and lines 34-38, "The cell monolayers were

Art Unit: 1631

subsequently analyzed by transferring the microscope image from a Zeiss axioplan microscope equipped with a x 40 objective and a 546 nm green filter to a SEP-IPS image processing unit (Kontron, Munich, Germany) using a Grundig FA 76 video camera. The nuclear boundaries were defined by the operator by establishing a threshold grey level for each image, and pixels darker than this threshold value were identified as belonging to a nucleus.... Visual identification in the grey level image and also in the microscope directly allowed the precise identification of cell types and also classification of nuclei as belonging to mononuclear or binuclear hepatocytes." Table 1 represents a processing and analysis of Figure 1A.

The features identified in Figure 1A of Geryling et al are nuclear features with given morphologies from which nuclei can be identified. Figure 1 allows the identification of nuclei not only from the staining, but also the presence of concave regions around each black nucleus. In bi-nuclear cells, where two nuclei are clustered, the bi-nucleus is represented by more than one concave region in which the spatial distribution of the nuclei represents whether a binucleus exists. The proximity of the two stained regions and the number of concave regions around the nuclei (i.e. nearest neighbour first features) indicates the presence of a binucleus. In addition, next nearest neighbor regions in Figure 1A were identified visually to determine the presence of multinuclear features.

The non-stained regions of Figure 1A indicate the presence of a cytoplasmic region. The absence of a cytoplasmic region between to stained nuclei indicates the presence of a binucleus. In other words, Figure 1A is used as a measure of the

Art Unit: 1631

cytoplasmic components of the cells from which the presence of binuclear cells can be identified. The intensities of the cytoplasmic versus nuclear component are binary in that the nuclei are gray while the cytoplasm is white. In Figure 1B, it is the opposite: cytoplasm is black while nuclei are white; the different types of stainings used in each Figure represent a different threshold for identifying bi-nuclear cells. Figure 1A represents normal hepatocytes while Figure 1B represents regenerated hepatocytes. The binucleation index for the regenerating liver is less than 4%. The difference between the number of nuclei in each picture is the effect of differences in cytokinesis between each cell type.

Figures 1A and 1B expose a population of cells to a plurality of treatments, capture images of the plurality of cells, obtain a plurality of features from the image, analyze the plurality of cellular features (which include nuclear and cytoplasmic features) to determine the presence of bi-nuclear features. Figures 1A and 1B show determination of bi-nuclear cells from two types of image analyses.

Table 1 shows the classification of treatments for normal liver versus regenerating liver cells as stated in the title, "Proliferation and binucleation of hepatocytes from regenerating and normal rat liver." Table 1 also applies a statistical test termed a "Binucleation index" indicating abundance of bi-nuclear cells in treated versus a controlled population.

However, Gerlyng does not teach the automation aspect of the image analysis.

The patent of Bacus, entitled "Method and an apparatus for image analysis of biological specimens," states in its abstract, "A user interactive system for dynamically

Art Unit: 1631

testing and evaluating various cells, antigens, or other materials taken from the human body. More specifically, the DNA in specimen cells is analyzed and quantified by image analysis using pattern recognition techniques. The user is provided with a unique slide or support on which there are simultaneously stained or otherwise image enhanced at the time of analysis." Figure 1 of Bacus illustrates such a computer system which uses automation to analyze the morphology of cells. As stated in column 11, lines 34-37 (claim 24 of Bacus), "A microscopic slide for an automated cell analysis system having stored known mass characteristics for cell objects and for use in analysis of specimen cell objects,..." Such an apparatus is "[an] improved method and apparatus for analyzing cells or other biological materials by using image analysis techniques."

[column 2, lines 66-68 of Bacus]

It would have been obvious to at the time of the instant invention to modify the manual binuclear imaging system of Gerlyng et al in view of the automated cell analysis system of Bacus because while both technique are utilized for image analysis of biological material, Bacus adds the advantage of automation and results in an improved set of image analysis techniques.

Claims 23-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 in further view of Rumbaugh [USPAT 4,821,210].

Claims 23-25 and 27 state:

23. A method for characterising cells, comprising: automatically determining, from a captured image of a nuclear component of a plurality of cells, the number of concave

Art Unit: 1631

portions in the outline of the image of the nuclear component; and automatically characterising the cell based on the number of concave portions.

24. The method as claimed in claim 23, further comprising smoothing the outline of the image of the nuclear component.

25. The method as claimed in claim 23, further comprising automatically identifying a concave portion in the outline of the image of the nuclear component by automatically determining the angle subtended by adjacent portions of the outline.

27. The method as claimed in claim 24, wherein smoothing the outline of the image of the nuclear component includes converting the outline into a polygon.

The methods of the base claim of characterizing cells are taught by Gerlyng et al. in view of Bacus.

However, Gerlyng et al. in view of Bacus does not teach fitting polygons to cellular structures.

In Rumbaugh, column 7, lines 48-53, it is stated, "generating for each test cell none, one or a set of polygonal representation surfaces which approximate the object corresponding to each cell, which polygons are then sequentially displayed based on a user defined viewplace or angle of viewing to cumulatively form the 3-D object or body."

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice Gerlyng et al in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 above, in view of Rumbaugh, because Rumbaugh teaches the advantage of using geometric analysis to simplify line shape around a cell.

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 in further view of Miyano et al [USPGPUB 2003/0108230].

Art Unit: 1631

Claims 23 and 24 state:

23. A method for characterising cells, comprising: automatically determining, from a captured image of a nuclear component of a plurality of cells, the number of concave portions in the outline of the image of the nuclear component; and automatically characterising the cell based on the number of concave portions.

24. The method as claimed in claim 23, further comprising smoothing the outline of the image of the nuclear component.

The methods of the base claim of characterizing cells are taught by Gerlyng et al. in view of Bacus.

However, Gerlyng et al. in view of Bacus does not teach smoothing the structures of the nuclei.

This additional limitation is taught in Miyano et al paragraph [0061] and Figure 11. The process of unifying nucleus area involves drawing an approximate circle around the nucleus as is shown in each picture in Figure 11.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice Gerlyng et al in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 above, in further view of Miyano et al, because Miyano et al teaches the advantage of using geometric analysis to smooth the area around a nucleus.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re*

Art Unit: 1631

Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-60 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-60 of copending Application No. 10/563,613. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims between the instant and applied application are identical in their entirety.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

Claims 1-60 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

For the reasons discussed above, it is apparent that copending Application No. 10/563,613 contains claimed subject matter in claims that is not patentably distinct from instant claim 1. Because the inventive entity of copending Application 10/563,613 is different from the instant application, a rejection is appropriate under 35 U.S.C. 102(f). This rejection could be overcome by amendment of the appropriate claims so that the claims are patentably distinct, or by filing a declaration stating the inventive entity for the commonly claimed subject matter is identical.

Response to Arguments

Applicant's arguments filed 13 July 2006 have been fully considered but they are not persuasive.

Applicant's arguments against the prior art rejections are on pages 13-16 of the "Remarks" of 13 July 2006. The arguments center on the difference of the claimed invention being executed automatically and the references being executed manually. This argument was addressed in this Office action by the addition of a reference which examines cells automatically which has a motivation to be combined with the original references.

Applicant argues against the 35 U.S.C. 102(f) rejection by stating that there is an intervening WIPO document between the reference document and the instant application with the identical inventive entity. However, the intervening document is inconsequential. The reference document (the national stage application) and that alone in compared with the instant application for double patenting. Since double patenting exists, and the inventive entities are distinct between both applications, the 35 U.S.C. 102(f) rejection is enacted by the Office.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

Art Unit: 1631

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Yolanda Chadwick, whose telephone number is (571) 272-0514.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

Application/Control Number: 10/615,116


Page 12

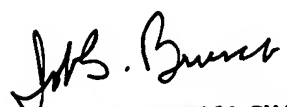
Art Unit: 1631

For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN

28 September 2006


28 September 2006

 29 September 2006
JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER